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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 16

Application Number: 09/501,714
Filing Date: February 10, 2000
Appellant(s): Au-Young et al.

Richard C. Ekstrom
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed March 8, 2002.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct.

(6) Issues

The appellant's statement of the issues in the brief is correct. The changes are as follows:

Issue 2 related to the rejection under 112, 1st paragraph, (enablement) of a probe comprising at least 16, 20, 30 or 60 contiguous nucleotides of SEQ ID NOs:2 or 4 or naturally-occurring polynucleotides which are 90% identical to SEQ ID NOs:2 or 4 is withdrawn by the examiner because one skilled in the art would know how choose and use a probe given the disclosure of a target sequence.

Issue 3 related to the rejection under 102 (a) over the EST taught by Hillier et al. (accession N93316) is withdrawn by the examiner in view of Appellants admission that "one must make the identity comparison to the **entire length** of SEQ ID NO:2" (page 16, 1st line).

Issues 4 and 5 related to the rejection under 102 (a) over any of the two ESTs taught by Hillier et al. (accession W63690 and accession AA020916) are withdrawn by the examiner in view of Appellants remarks in connection with the 102 rejection based

on Hillier et al. N93316 (Issue 3) and because only a fragment of said ESTs has more than 90% identity to SEQ ID NO: 4. The entire ESTs are less than 90% identical to SEQ ID NO:4.

Issue 6 related to the rejection under 102 (b) over the EST taught by Weissenbach (accession Z52396) is withdrawn by the examiner in view of Appellants remarks in connection with the 102 rejection based on Hillier et al. N93316 (Issue 3) and because only a fragment of said EST has more than 90% identity to SEQ ID NO: 2. The entire EST is less than 90% identical to SEQ ID NO:2.

Issue 7 in part related to the rejection under 103 (a) over the EST taught by Weissenbach (accession Z52396) is withdrawn by the examiner because said EST would not be useful as a specific probe for detecting a polynucleotide of SEQ ID NO:2 in view of its overall low homology to SEQ ID NO: 2.

(7) Grouping of Claims

The appellant's statement in the brief that claims stand or fall together for each of the issues on appeal is correct.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Hillier et al. (20 Aug 1996) (Database EST, accession N93316).
Hillier et al. (11 Oct 1996) (Database EST, accession W63690).
Hillier et al. (30 Jan 1997) (Database EST, accession AA020916).

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim 45, with dependent claims 47-49, and claim 52, with dependent claims 54-56 and 66-68, stand finally rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to or depend from a genus of naturally-occurring polynucleotides which are 90% identical to SEQ ID NOs:2 or 4 and probes comprising at least 16, 20, 30 or 60 nucleotides thereof; or a genus of polynucleotides encoding naturally-occurring amino acid sequences that are 90% identical to SEQ ID NOs:1 or 3.

Thus, said genus encompasses all allelic variants of SEQ ID NOs: 2 or 4. There is no limitation on the function of the encoded protein. Thus, the genera of

polynucleotides of claims 45, 47-49, 52, 54-56 and 66-68 encompass polynucleotides encoding proteins having DnaJ chaperone activity and many inactive variants thereof.

Allelic variants are alternate forms of a gene which have at least one mutation in the nucleotide sequence which may result in mRNAs (polypeptides) with altered function. With regard to a naturally-occurring human polynucleotide sequence variant, there is no description in the specification of any mutational site that exist in nature, and there is no description of how the structure of SEQ ID NOs:2 or 4 relates to the structure of any allele including strictly neutral alleles. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others.

In the instant case the claimed genera of Claims 45b and 52b includes species which are widely variant in function. Naturally occurring amino acid sequences having at least 90% identity to SEQ ID NOs:1 or 3, includes allelic variants of SEQ ID NOs:1 or 3 and all other loci which encode proteins having 90% identity to SEQ ID NOs:1 or 3. Allelic variants encode polypeptides **whose function may or may not be altered**. The above genus of polypeptides is functionally diverse as it encompasses polypeptides with DnaJ chaperone activity and those which lack such activity but possibly have other undisclosed functions. As such, neither the description of the structure and function of

SEQ ID NOs:1 or 3 nor the disclosure solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Claims 54-56 and 66 are drawn to a method of use of a diverse genus of a probe comprising at least 16, 20, 30 or 60 contiguous nucleotides comprising a sequence complementary to SEQ ID NO: 2 or SEQ ID NO: 4 or a naturally-occurring polynucleotide having at least 90% sequence identity to SEQ ID NO: 2 or SEQ ID NO: 4 (a polynucleotide of claim 52). The considerations discussed above with regard to the full-length sequences also apply to probes that comprise a number of contiguous nucleotides of said full-length sequences.

Therefore, one of skill in the art would not conclude that applicant was in possession of the claimed genus because a description of only one member of this

genus is not representative of the variants of the genus and is insufficient to support the claims.

Claims 54 and 66 stand finally rejected under 35 U.S.C. 103(a) as being unpatentable over any of Hillier et al. (accession N933160, accession W63690 or accession AA020916).

Hillier et al. (accession N93316) teach an EST of 482 bp that has 99.2% identity to nucleotides 817-1298 of SEQ ID NO:2. They teach that said EST is homologous to DnaJ.

Hillier et al. (accession W63690) teach an EST of 661 bp that has 93.6% identity to nucleotides 23-618 of SEQ ID NO:4. They teach that said EST is homologous to DnaJ.

Hillier et al. (accession AA020916) teach an EST of 646 bp that has 94.6% identity to nucleotides 26-638 of SEQ ID NO:4.They teach that said EST is homologous to DnaJ.

Each of these EST sequences comprises at least 16, 20, 30 and 60 contiguous nucleotides of SEQ ID NO:2 or SEQ ID NO:4 and is a fragment of a human cDNA encoding a portion of a human DnaJ protein. Furthermore, these ESTs are complementary to a polynucleotide of claim 52 because "complementary" as defined in

the specification does not require for a probe to be a fragment of a given polynucleotide, i.e. to be fully, or 100%, complementary thereto (page 10, lines 13-21).

Therefore, as knowledge of all the genes encoded by the human genome is important for understanding and/diagnosing human diseases or genetically determined drug interactions and for understanding many other human cellular processes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use these cDNA fragments as hybridization probes for detecting a full-length target polynucleotide that specifically hybridizes thereto in the presence and absence of test compounds. Given the presence of SEQ ID NO:2 or SEQ ID NO:4 in a sample, it will specifically hybridize with any of the DNA fragments of Hillier et al.

Claims 45-49 and 52 stand finally rejected under the judicially created doctrine of double patenting over claims 1-9 of U. S. Patent No. 5,922,567 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent. While claims 45-49 and 52 are of different scope than claims 1-9 of U. S. Patent No. 5,922,567, they encompass the polynucleotides to which claims 1-9 of U. S. Patent No. 5,922,567 are drawn (a polynucleotide encoding SEQ ID NO:1 and SEQ ID NO:2). A terminal disclaimer is required because claims 45-49 and 52 include the polynucleotides that are already covered by the issued patent.

Claims 45-49 and 52 stand finally rejected under the judicially created doctrine of double patenting over claims 1-9 of U. S. Patent No.6,001,598 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent. While claims 45-49 and 52 are of different scope than claims 1-9 of U. S. Patent No. 6,001,598, they encompass the polynucleotides to which claims 1-9 of U. S. Patent No. 6,001,598 are drawn (a polynucleotide encoding SEQ ID NO:3 and SEQ ID NO:4). A terminal disclaimer is required because claims 45-49 and 52 include the polynucleotides that are already covered by the issued patent.

Applicants' consideration for filing a TD stated in Remarks filed March 12, 2001 and in Brief on Appeal filed March 8, 2002 is noted.

(11) Response to Argument

Appellants argue that the rejection of the claims 45, 47-49, 52, 54-56 and 66-68 under 35 U.S.C. 112, 1st paragraph (written description), is improper "as the claims define subject matter which is described in the Specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed subject matter at the time the application was filed" (page 7, 1st paragraph). Appellants further argue that "the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art. ... SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4 are specifically disclosed

in the application (see, for example, the Specification at page 15, line 20 through page 16, lin 19; Sequence Listing at pages 57-60; Figures 1A through 1D; and Figures 3A through 3D). Polypeptide variants having at least 90% identity to SEQ ID NO:1 and SEQ ID NO:3 are described, for example, at page 16, lines 20-23" (page 8). This is not agreed with because polynucleotides encoding SEQ ID NO:1 and SEQ ID NO:3 are not rejected and the application at the indicated pages does not disclose naturally-occurring variants but any variants. Appellants further argue that "30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues" and further "naturally-occurring molecules may exist which could be characterized as DnaJ-like proteins "(pages 10 and 11). This is not agreed with because the claims are not drawn specifically to polynucleotides encoding naturally-occurring DnaJ-like proteins but to a genus comprising polynucleotides encoding naturally-occurring proteins having DnaJ-like activity as well as inactive variants thereof or proteins having an undisclosed activity. While one skilled in the art is enabled to detect such naturally-occurring sequences, it is impossible to visualize them without knowing the correlation between SEQ ID NO:2 or SEQ ID NO:4 and mutational sites. Appellants assert that the state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications (page 11, last two paragraphs). While the advances in the art are undeniable and widely recognized, the point of the rejection is the description not the enablement. The art still

does not allow to predict the structure of existing naturally-occurring variants based on the single structure. Most importantly, one skilled in the art would not be able to predict possibly diverse functions of other naturally-occurring sequences based on the knowledge of the function of only one species.

With regard to the written description of the probes Appellants argue that claims 54-56 and 66 are "drawn to a method of use of a probe comprising at least 16, 20, 30 and 60 contiguous nucleotides of [SEQ ID NO:2 or SEQ ID NO:4]" (page 12, 2nd paragraph, emphasis added). Appellants continue "Support for such use of nucleic acid sequences of this type can be found, for example, in the Specification at page 13, lines 9-13 ... and their function is to bind to the complimentary portion of the target polynucleotide in the sample" (page 12, 2nd paragraph). As discussed above, a genus of probes lack written description because the full-length target sequences lack sufficient written description.

With regard to the 103(a) rejection of claims 54 and 66 Appellants argue that "The Office Action did not provide an explanation of any differences between the claim and the applied art, or any proposed modification of the applied references necessary to arrive at the claimed subject matter. Furthermore, the Examiner did not provide any suggestion of the desirability of doing what the inventors have done" (page 19). And further "The Examiner has completely ignored that claim [17] 54 is directed to a method

of detecting a target nucleotide having the sequence of a polynucleotide of claim 52. ... None of the applied art provides any description or recognition of a target polynucleotide having a sequence as set forth by claim 52 " (page 20, last three paragraphs). This is disagreed with. It appears that the essence of disagreement between Appellants and the examiner is that Appellants consider a method for detecting a product as an independent category of methods. And a method for detecting a novel and non-obvious product (a polynucleotide of claim 52) as a novel and non-obvious method as result of this. However, said product is detected by a method that is a method of use of another product. The examiner position is that a method for detecting a product is novel and non-obvious as long as it is a method of use of a novel and non-obvious product. The product used in methods of claims 54 and 66 is known in the art. The examiner notes, that claims 54 and 66 recite a probe comprising at least 16 and 20 contiguous nucleotides, respectively, of the polynucleotide of claim 52. The sequences disclosed by Hillier et al. meet such limitations. The method for detecting a polynucleotide of claim 52 using a probe that consists of at least 20 contiguous nucleotides of the polynucleotide of SEQ ID NO:2 is novel and non-obvious.

A method of use of the Hillier et al. sequences would result in detecting any sequence that will hybridize therewith including the sequences of claim 52. This depends on nucleotides present in the sample. Samples in which the sequences of

claim 52 are present are of interest to the inventors and will be chosen. While the detecting the sequences that are encompassed by claim 52 is a goal, the methods of claims 54 and 66 are methods of use of a probe known in the art. The methods are enabled and obvious. The motivation and expectation of success are provided by the references and the art because the whole reason for creating databases containing partial nucleotide sequences is to use them for detecting full length sequences.

Appellants do not argue the double patenting rejection of claims 45-49 and 52 over claims of U.S. Patent No. 5,922,567 and U.S. Patent No.6,001,598. Appellants consideration for filing Terminal Disclaimers is noted. The claims stand rejected until TDs are filed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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May 28, 2002

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